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=> d his

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L1                STRUCTURE UPLOADED
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L3             1 S L1 OR L2
L4            22 S L3 FULL

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L5             2 S L4

=> d que l5 stat
L1                STR
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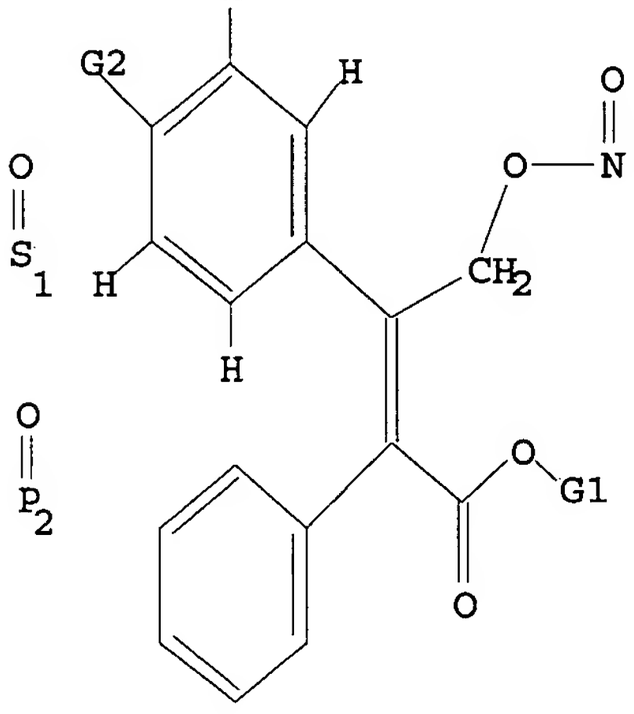


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G1 H,Cy,Ak
G2 [@1],[@2]

Structure attributes must be viewed using STN Express query preparation.
L2                STR
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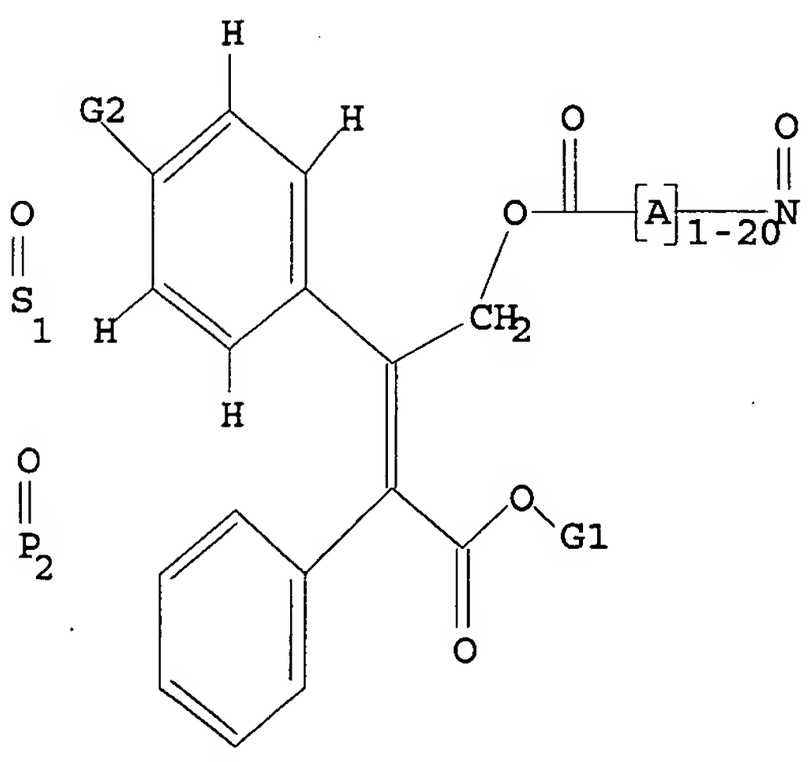


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G1 H,Cy,Ak
G2 [@1],[@2]
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Structure attributes must be viewed using STN Express query preparation.
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L5 2 SEA FILE=CAPLUS ABB=ON PLU=ON L4

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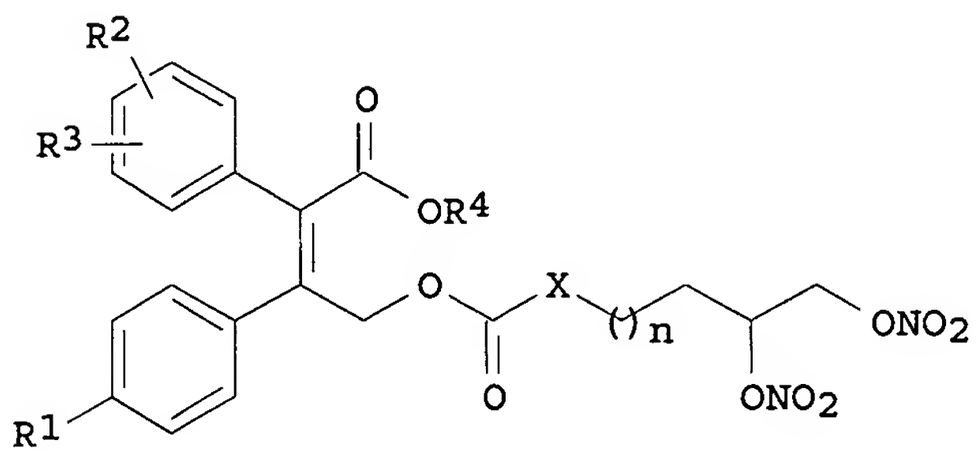
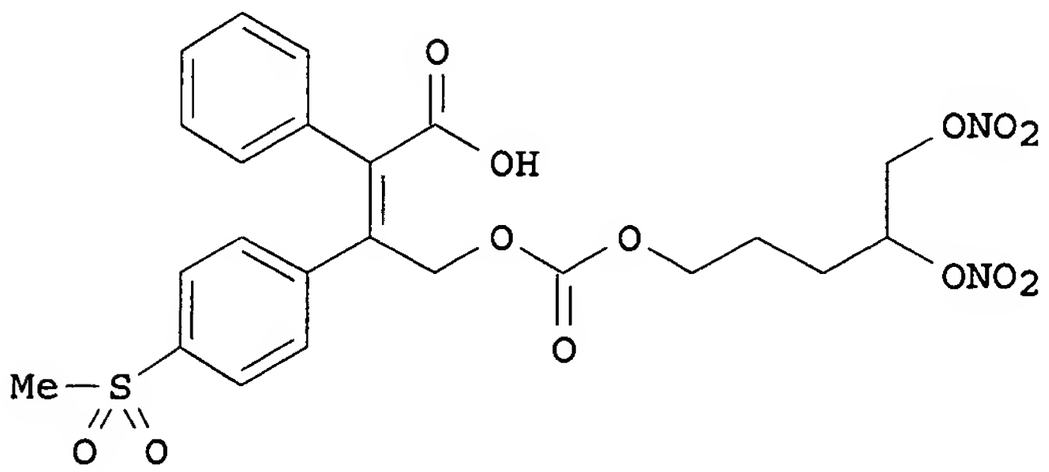
L5 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:696873 CAPLUS
DN 143:172624
TI Preparation of nitric oxide releasing prodrugs of diaryl-2(5H)-furanones as cyclooxygenase-2 inhibitors
IN Dufresne, Claude; Berthelette, Carl; Li, Lianhai; Guay, Daniel; Gallant, Michel; Lacombe, Patrick; Aspiotis, Renee; Wang, Zhaoyin; Sturino, Claudio F.
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005070883	A1	20050804	WO 2005-CA83	20050125
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2004-539666P	P	20040127		

OS MARPAT 143:172624
GI



I



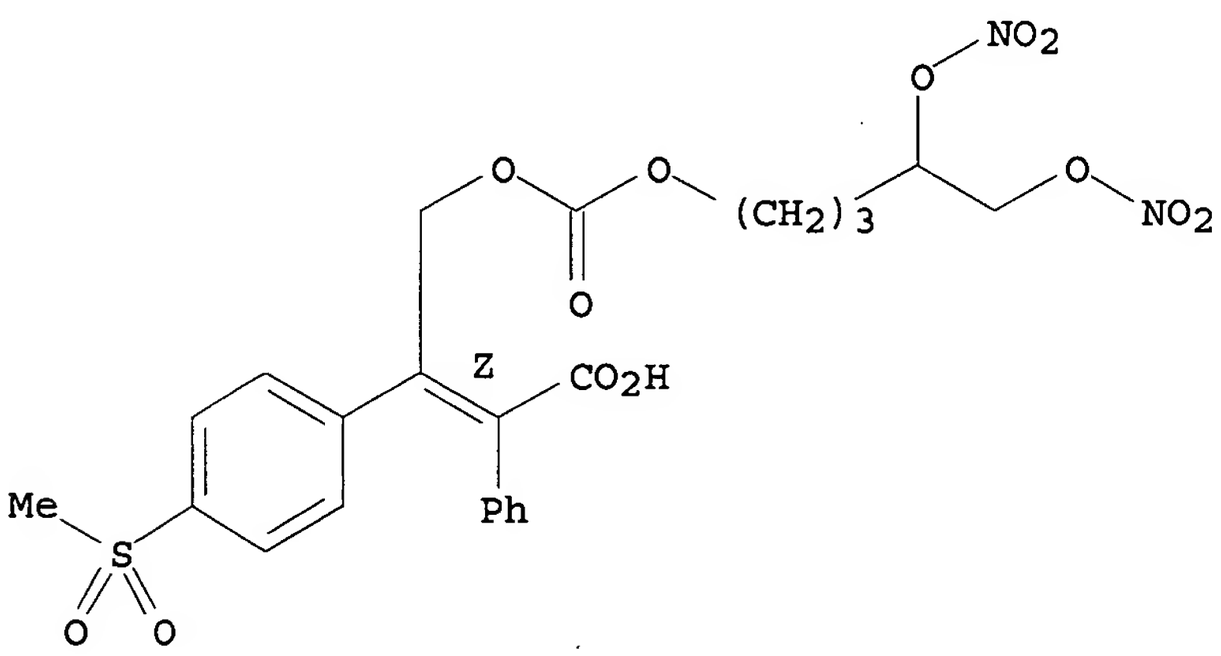
II

AB Nitric oxide-releasing prodrugs I [X = O, CH2; n = 1-6; R1 = SO2CH3, SO2NH2; R2-3 = H, halo, alkoxy, etc.; R4 = H, alkyl, etc.] are prepared For instance, II is prepared in several steps from 3,4-bis(nitrooxy)butyl alc., phosgene and (Z)-4-[(tert-butyldimethylsilyl)oxy]-2-[4-(methylsulfonyl)phenyl]-3-phenylbut-2-en-1-ol. I are useful for the treatment of cyclooxygenase-2 mediated diseases alone and in combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases or conditions while also reducing the risk of thrombotic cardiovascular events [no data].

IT 861430-32-2P 861430-35-5P
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of nitric oxide releasing prodrugs of diaryl-2(5H)-furanones as cyclooxygenase-2 inhibitors)

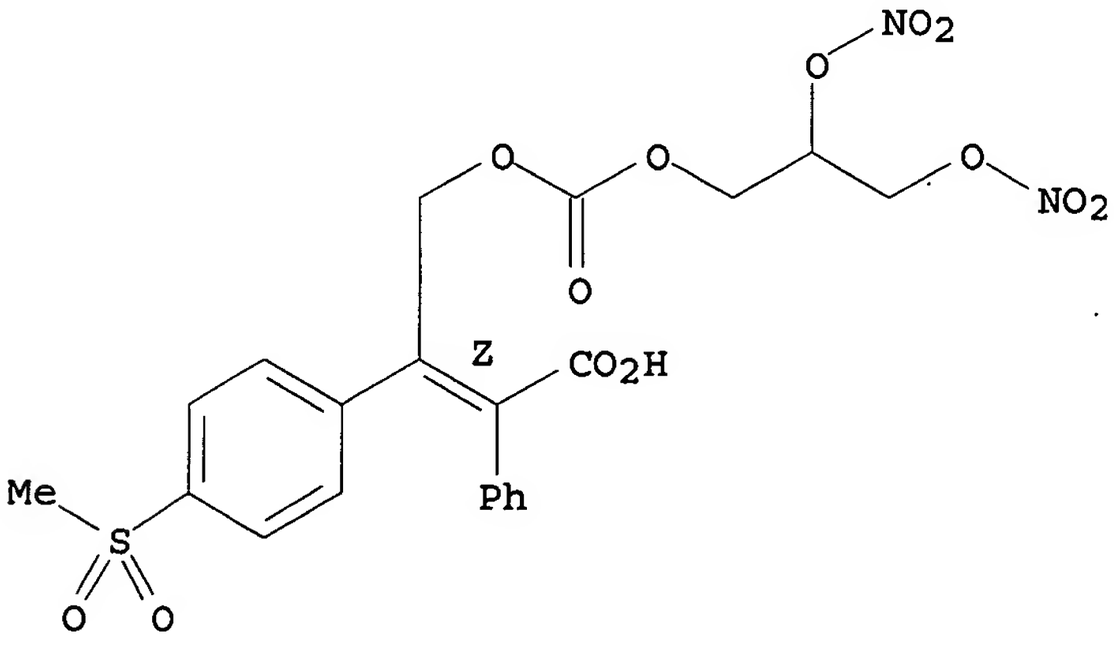
RN 861430-32-2 CAPLUS
CN Benzeneacetic acid, α-[2-[[[[4,5-bis(nitrooxy)pentyl]oxy]carbonyl]oxy]-1-[4-(methylsulfonyl)phenyl]ethylidene]-, (αZ)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 861430-35-5 CAPLUS
CN Benzeneacetic acid, α-[2-[[[2,3-bis(nitrooxy)propoxy]carbonyl]oxy]-1-[4-(methylsulfonyl)phenyl]ethylidene]-, (αZ)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



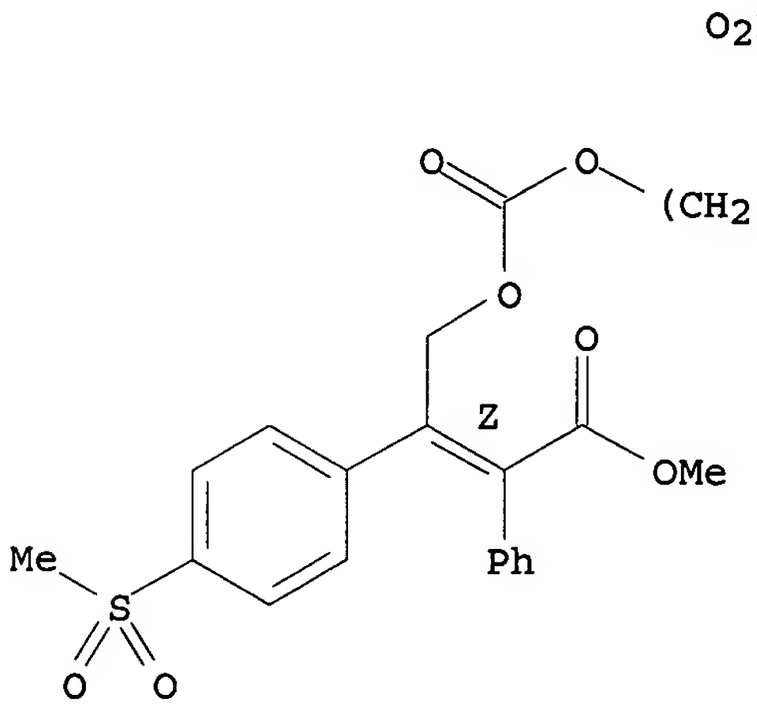
IT 861430-33-3P 861430-34-4P 861430-36-6P
861430-38-8P

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitric oxide releasing prodrugs of diaryl-2(5H)-furanones as cyclooxygenase-2 inhibitors)

RN 861430-33-3 CAPLUS

CN Benzeneacetic acid, α-[2-[[[[4,5-bis(nitrooxy)pentyl]oxy]carbonyl]oxy]-1-[4-(methylsulfonyl)phenyl]ethylidene]-, methyl ester, (αZ)- (9CI) (CA INDEX NAME)

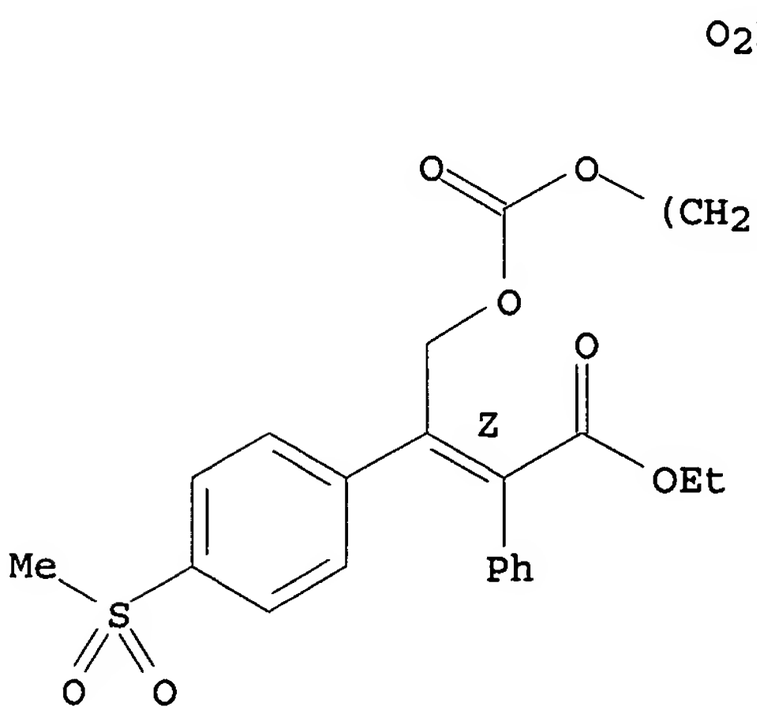
Double bond geometry as shown.



RN 861430-34-4 CAPLUS

CN Benzeneacetic acid, α-[2-[[[[4,5-bis(nitrooxy)pentyl]oxy]carbonyl]oxy]-1-[4-(methylsulfonyl)phenyl]ethylidene]-, ethyl ester, (αZ)- (9CI) (CA INDEX NAME)

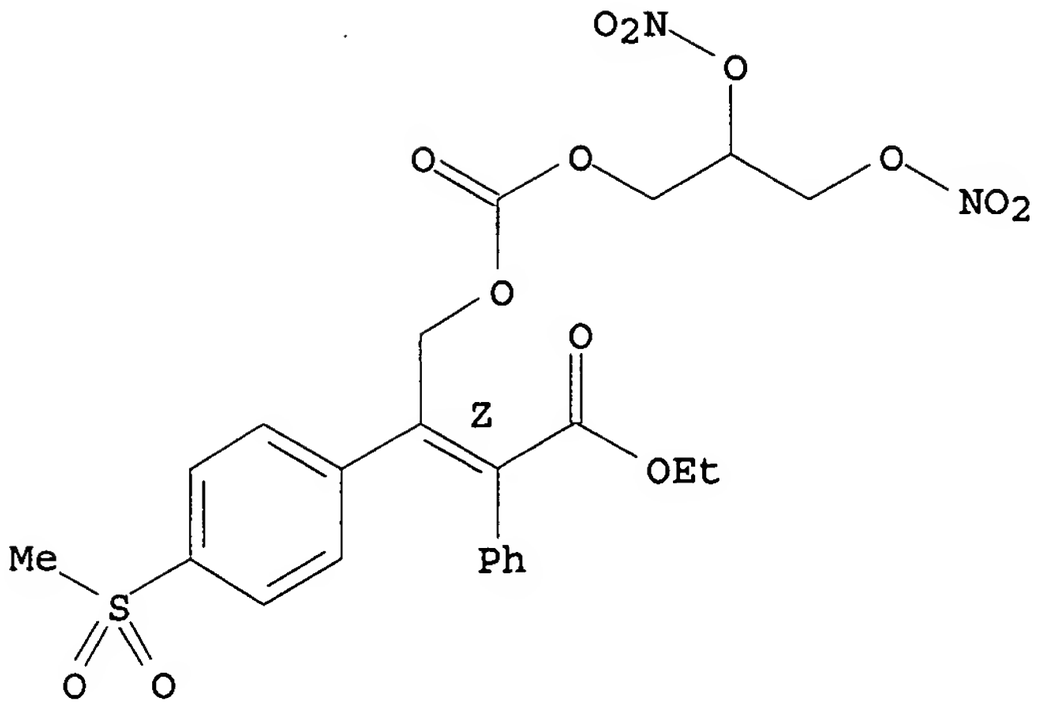
Double bond geometry as shown.



RN 861430-36-6 CAPLUS

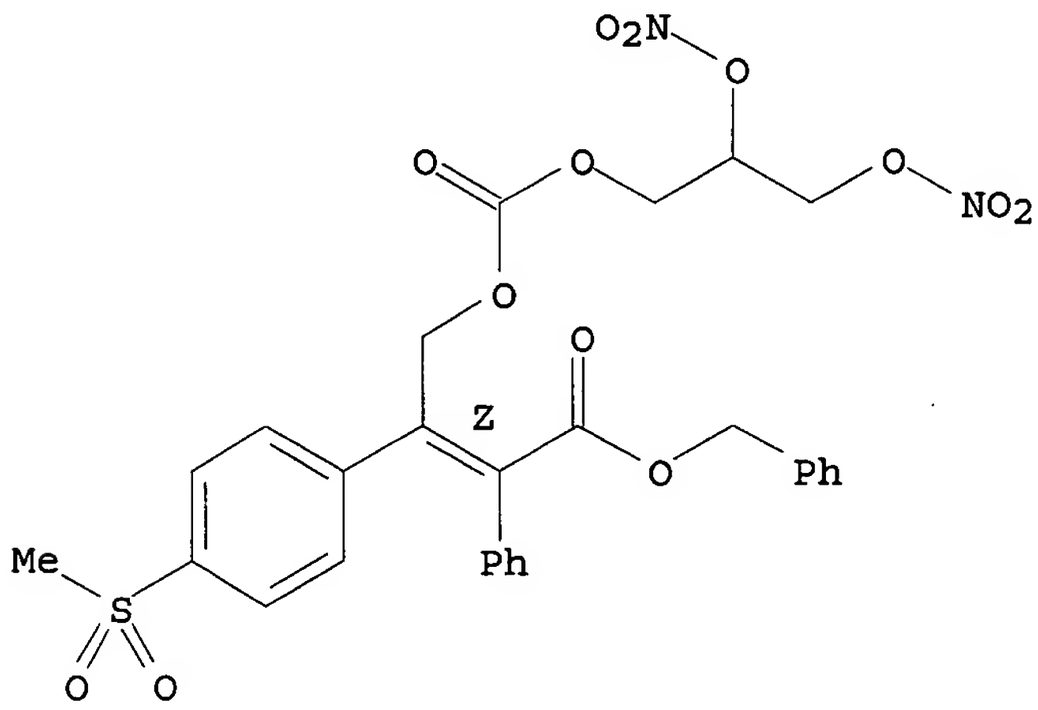
CN Benzeneacetic acid, α-[2-[[[2,3-bis(nitrooxy)propoxy]carbonyl]oxy]-1-[4-(methylsulfonyl)phenyl]ethylidene]-, ethyl ester, (αZ)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 861430-38-8 CAPLUS
CN Benzeneacetic acid, α-[2-[[[2,3-bis(nitrooxy)propoxy]carbonyl]oxy]-1-[4-(methylsulfonyl)phenyl]ethylidene]-, phenylmethyl ester, (αZ)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:101124 CAPLUS
DN 140:163574
TI Preparation of nitric oxide releasing diaryl-2-(5H)-furanone prodrugs as selective cyclooxygenase-2 inhibitors for treatment inflammatory diseases
IN Berthelette, Carl; Lachance, Nicholas; Li, Lianhai; Sturino, Claudio; Wang, Zhaoyin; Young, Robert N.; Dufresne, Claude
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004011421	A1	20040205	WO 2003-CA1115	20030724
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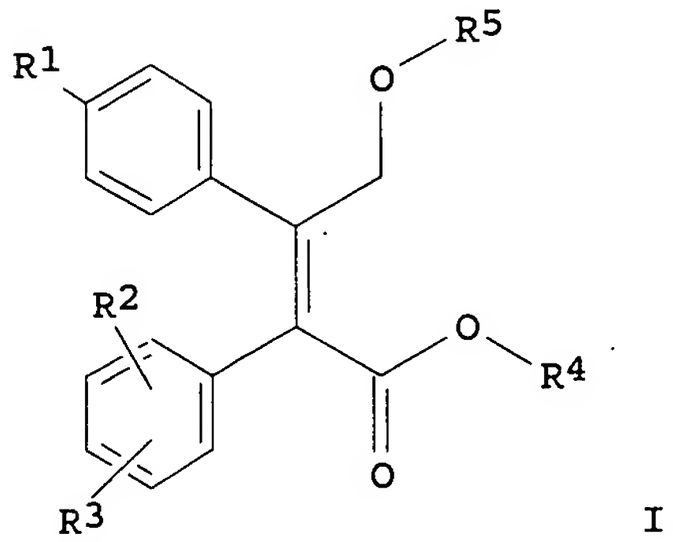
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2493082	AA	20040205	CA 2003-2493082	20030724
	AU 2003252515	A1	20040216	AU 2003-252515	20030724
	EP 1527045	A1	20050504	EP 2003-771010	20030724
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2005261245	A1	20051124	US 2005-521075	20050112
PRAI	US 2002-398683P	P	20020726		
	US 2002-435341P	P	20021220		
	WO 2003-CA1115	W	20030724		

OS MARPAT 140:163574
GI



I

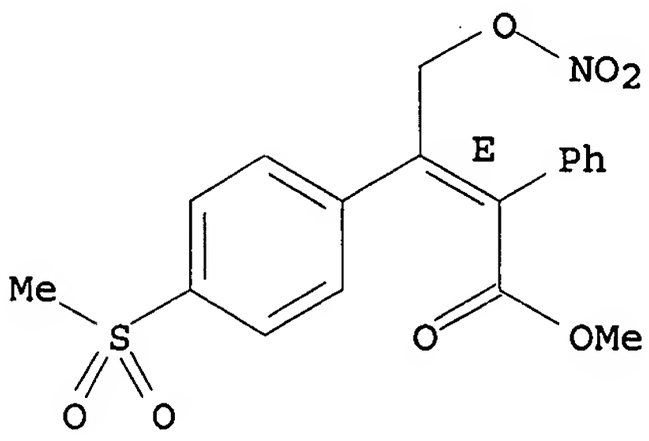
AB Title compds. I [R1 = S(O)2CH3, S(O)2NH2, S(O)2NHC(=O)CF3, etc.; R2, R3 = H, halo, alkoxy, etc.; R4 = H, (un)substituted alkyl, e.g., halo, Ph, naphthyl, etc.; R5 = NOx, C(=O)-E-alkyl-W-NOx, C(=O)-E-alkyl-Ar-alkyl-W-NOx; x = 1, 2; E = bond, O, S, etc.; W = O, S, C[CO2Rb]2; Ar = (un)substituted Ph, naphthyl, HET3; HET3 = benzimidazolyl, benzofuranyl, benzopyrazolyl, etc.; Rb = (un)substituted alkyl, Ph, naphthyl, etc.] and their pharmaceutically acceptable salts were prepared For example, allylic bromination of Me (2E)-3-[4-(methylsulfonyl)phenyl]-2-phenylbut-2-enoate, e.g., prepared from 1-(4-methanesulfonylphenyl)ethanone in 2 steps, followed

by O-alkylation of AgNO3 afforded nitrate ester I [R1 = 4-S(O)2CH3; R2, R3 = H; R4 = CH3; R5 = NO2] in 23% overall yield. In human whole blood LPS induced PGE2 and TXB2 production assays, compds. I have a COX-2 potency and COX-2/COX-1 selectivity comparable to rofecoxib. In paw edema assays in rat, compound I [R1 = 4-S(O)2CH3; R2, R3 = H; R4 = CH3; R5 = CO2(CH2)4ONO2] exhibited 42-79% inhibition of pain at 1-30 mg/kg dosage. Of note, compds. I are prodrugs of rofecoxib analogs and are claimed useful for the treatment of chronic COX-2 mediated diseases, while reducing the risk of thrombotic cardiovascular events. Compds. I are useful for treatments of osteoarthritis, rheumatoid arthritis, and chronic pain.

IT 654069-13-3P
RL: BYP (Byproduct); PREP (Preparation)
(preparation of nitric oxide releasing diarylfuranone prodrugs as selective cyclooxygenase-2 inhibitors for treatment of inflammatory diseases)

RN 654069-13-3 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-(nitrooxy)ethylidene]-, methyl ester, (αE)- (9CI) (CA INDEX NAME)

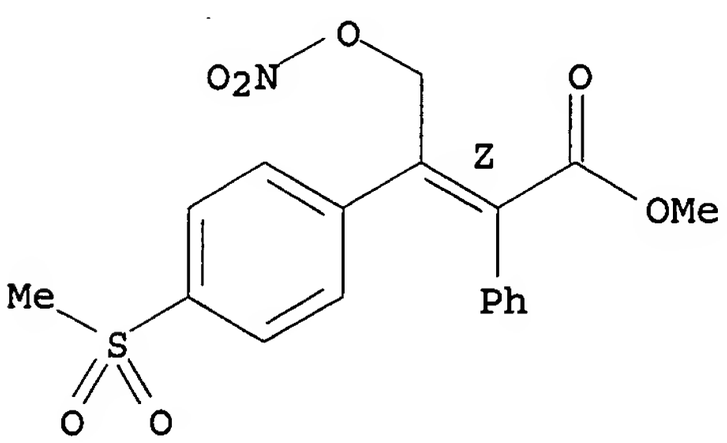
Double bond geometry as shown.



IT 654068-74-3P 654068-76-5P 654068-77-6P
654068-79-8P 654068-81-2P 654068-82-3P
654068-83-4P 654068-84-5P 654068-85-6P
654068-86-7P 654068-87-8P 654068-88-9P
654068-89-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitric oxide releasing diarylfuranone prodrugs as selective cyclooxygenase-2 inhibitors for treatment of inflammatory diseases)

RN 654068-74-3 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-(nitrooxy)ethylidene]-, methyl ester, (αZ)- (9CI) (CA INDEX NAME)

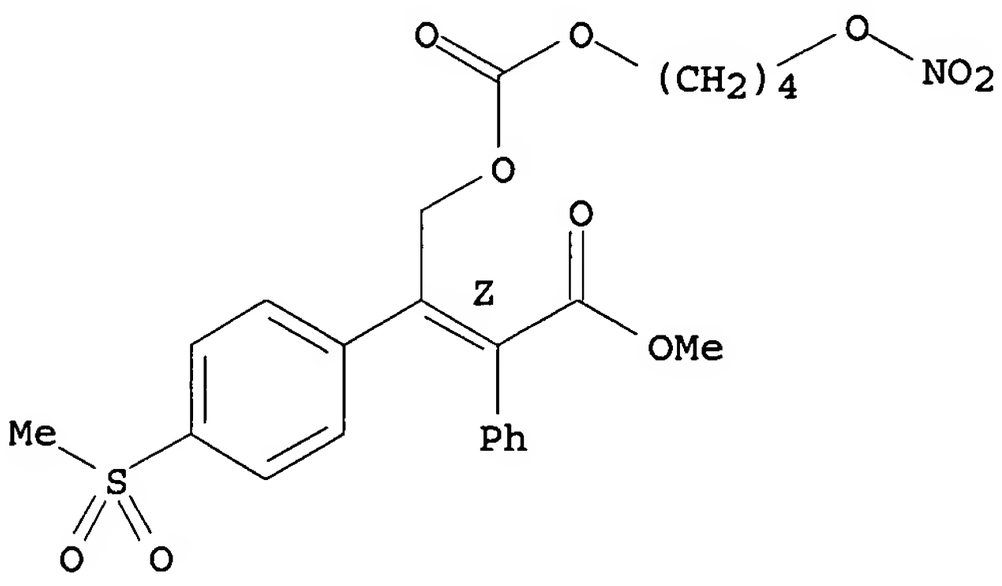
Double bond geometry as shown.



RN 654068-76-5 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[[4-

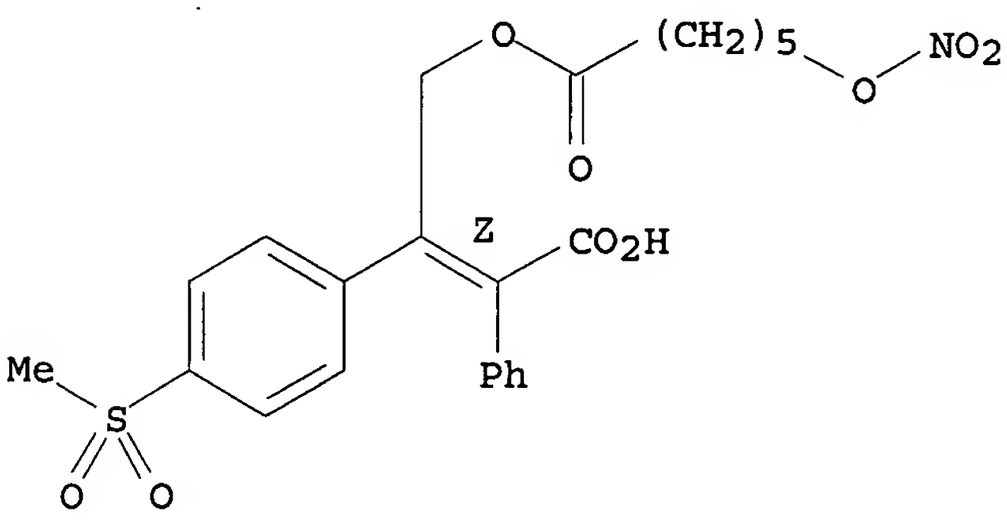
(nitrooxy)butoxy]carbonyl]oxy]ethylidene]-, methyl ester, (αZ)-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.



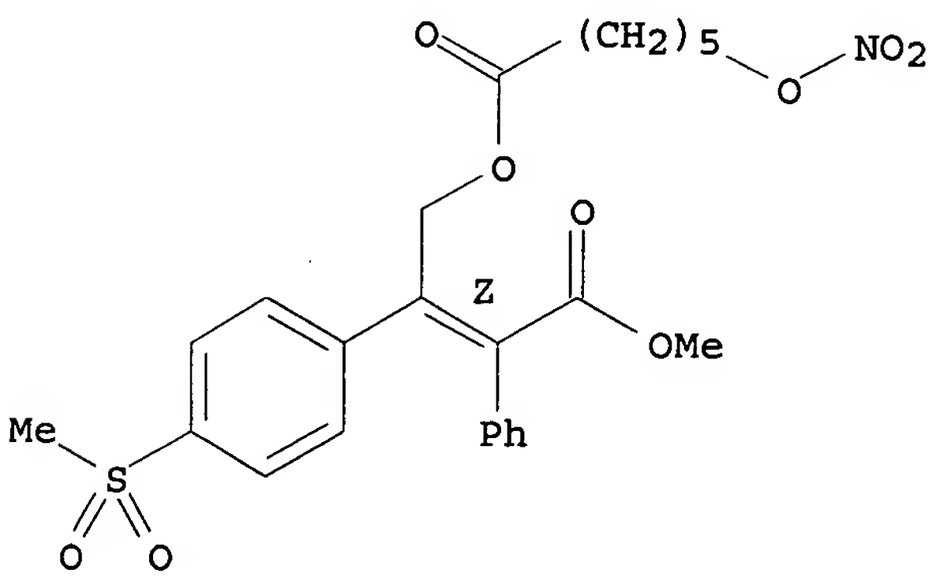
RN 654068-77-6 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[6-(nitrooxy)-1-oxohexyl]oxy]ethylidene]-, (αZ)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 654068-79-8 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[6-(nitrooxy)-1-oxohexyl]oxy]ethylidene]-, methyl ester, (αZ)- (9CI) (CA INDEX NAME)

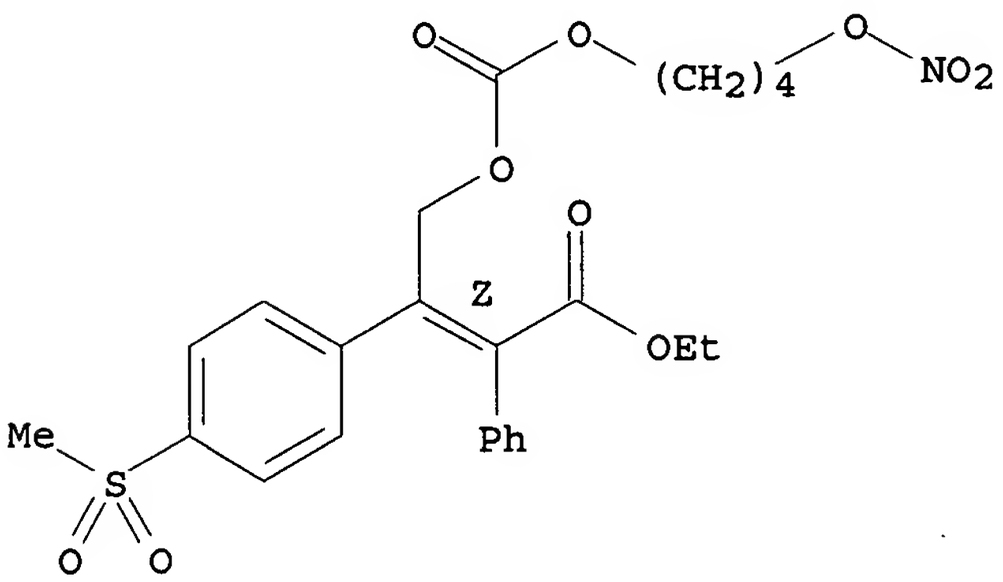
Double bond geometry as shown.



RN 654068-81-2 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[[4-

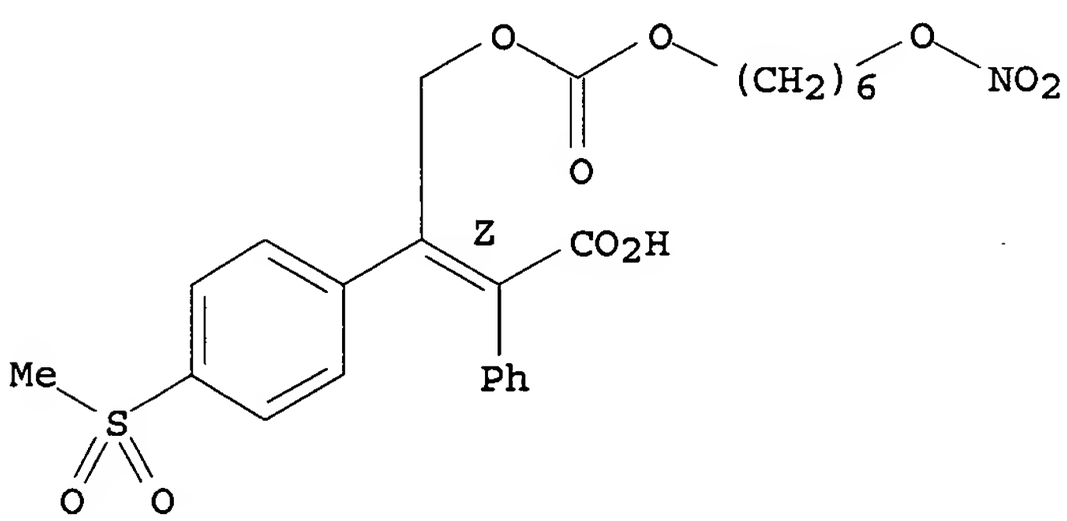
(nitrooxy)butoxy]carbonyl]oxy]ethylidene]-, ethyl ester, (αZ)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



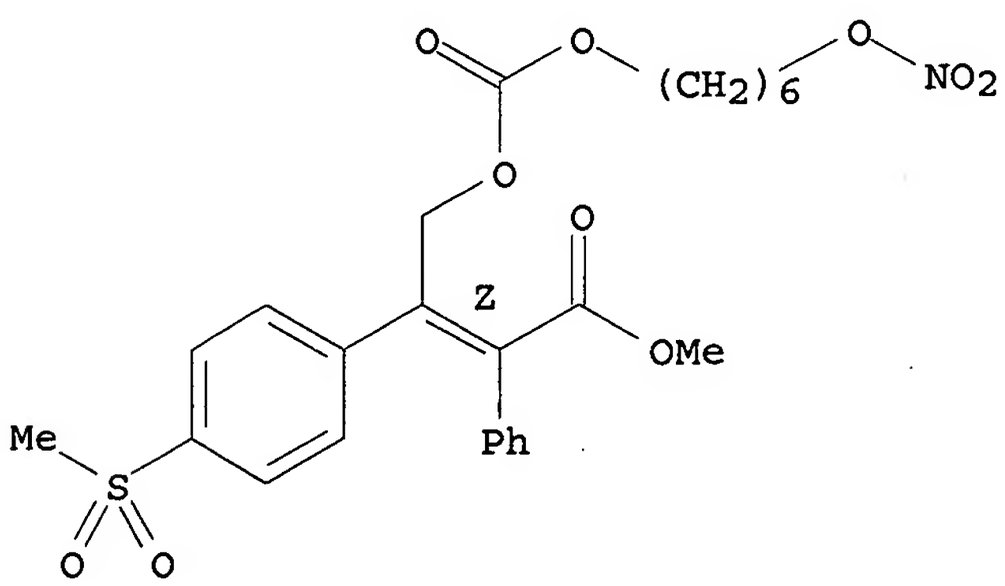
RN 654068-82-3 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[[[6-(nitrooxy)hexyl]oxy]carbonyl]oxy]ethylidene]-, (αZ)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 654068-83-4 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[[[6-(nitrooxy)hexyl]oxy]carbonyl]oxy]ethylidene]-, methyl ester, (αZ)- (9CI) (CA INDEX NAME)

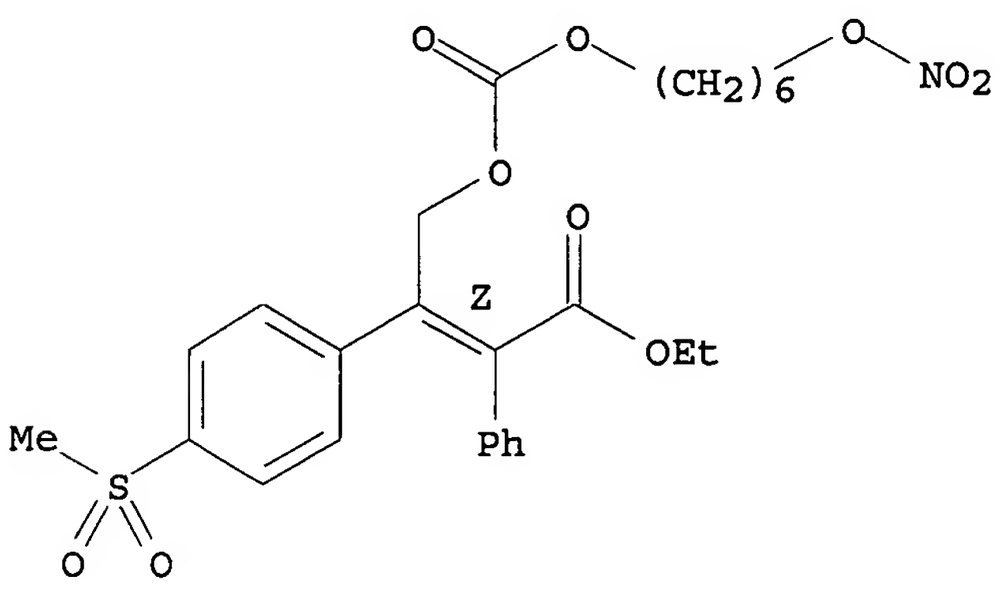
Double bond geometry as shown.



RN 654068-84-5 CAPLUS

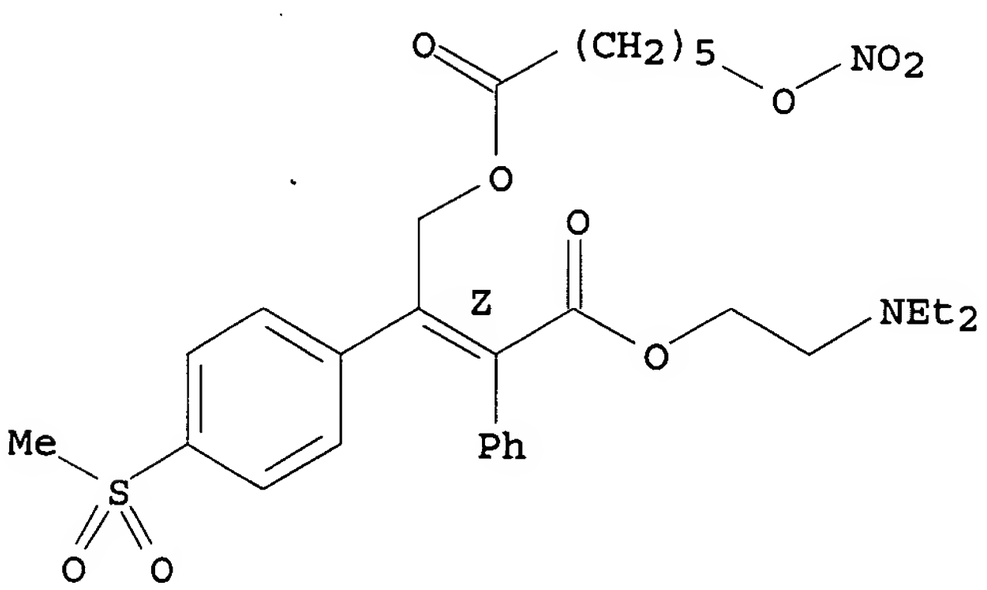
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[[[6-(nitrooxy)hexyl]oxy]carbonyl]oxy]ethylidene]-, ethyl ester, (αZ)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



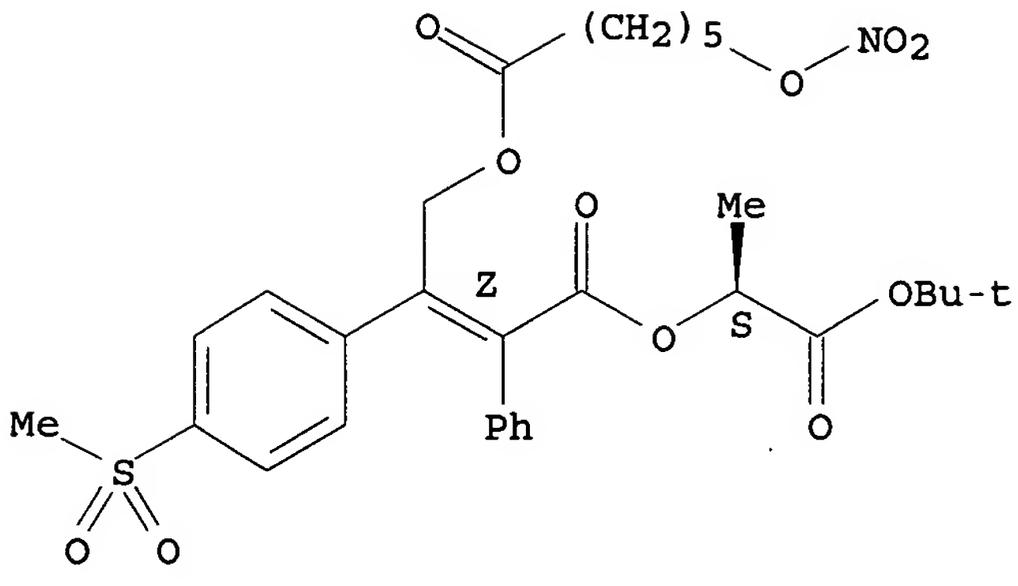
RN 654068-85-6 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[6-(nitrooxy)-1-oxohexyl]oxy]ethylidene]-, 2-(diethylamino)ethyl ester, (αZ)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



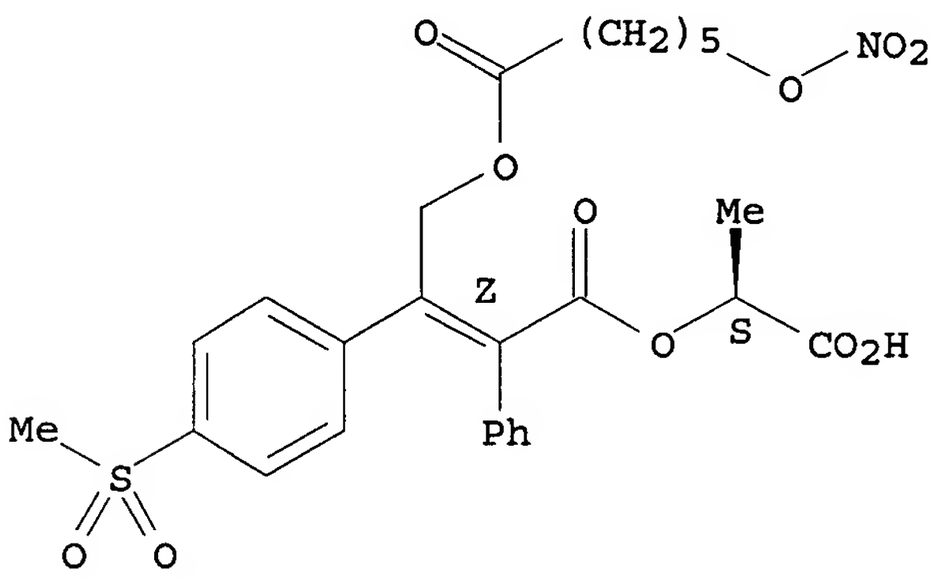
RN 654068-86-7 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[6-(nitrooxy)-1-oxohexyl]oxy]ethylidene]-, (1S)-2-(1,1-dimethylethoxy)-1-methyl-2-oxoethyl ester, (αZ)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



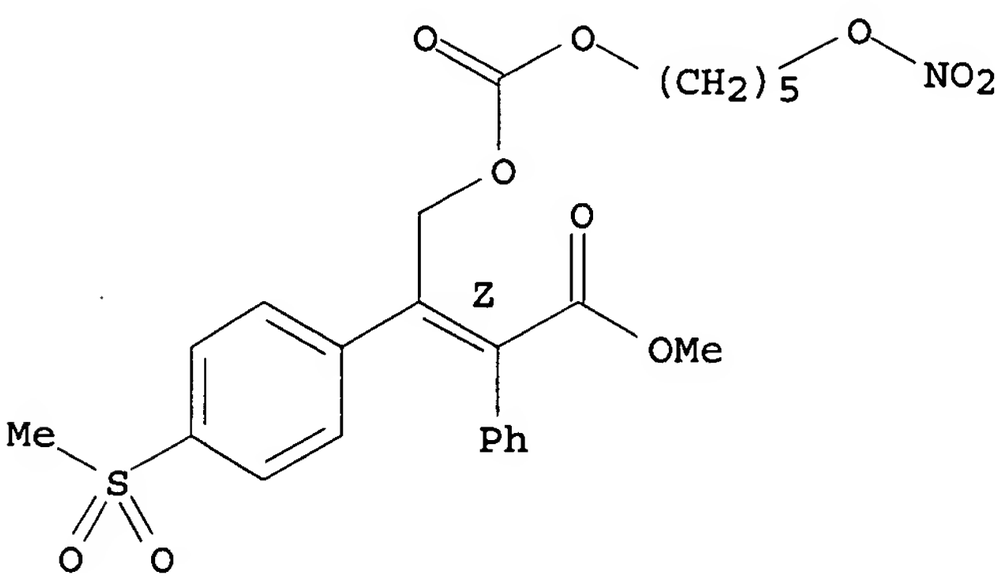
RN 654068-87-8 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[6-(nitrooxy)-1-oxohexyl]oxy]ethylidene]-, (1S)-1-carboxyethyl ester, (αZ)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 654068-88-9 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[[[5-(nitrooxy)pentyl]oxy]carbonyl]oxy]ethylidene]-, methyl ester, (αZ)- (9CI) (CA INDEX NAME)

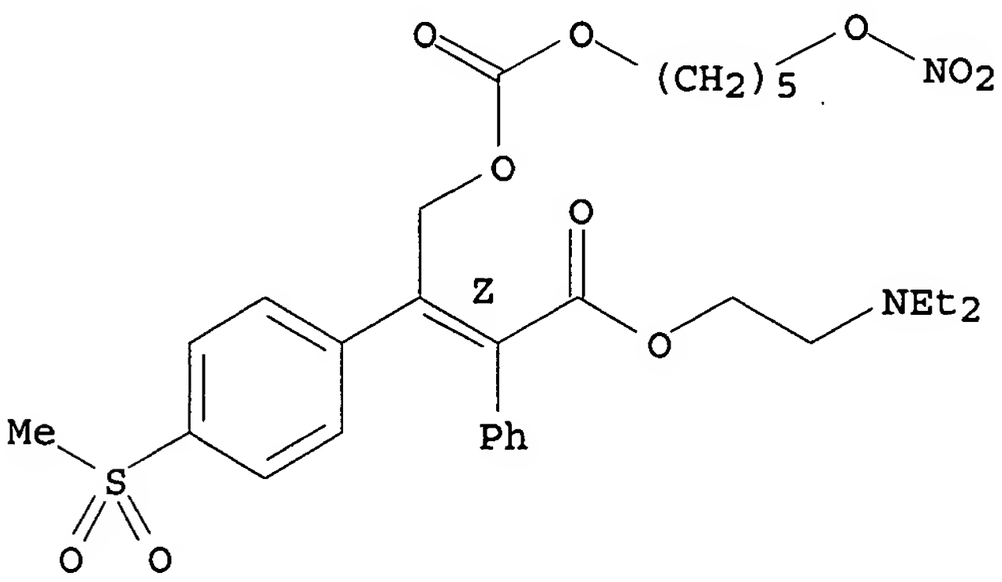
Double bond geometry as shown.



RN 654068-89-0 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[[[5-

(nitrooxy)pentyl]oxy]carbonyl]oxy]ethylidene]-, 2-(diethylamino)ethyl ester, monohydrochloride, (αZ)- (9CI) (CA INDEX NAME)

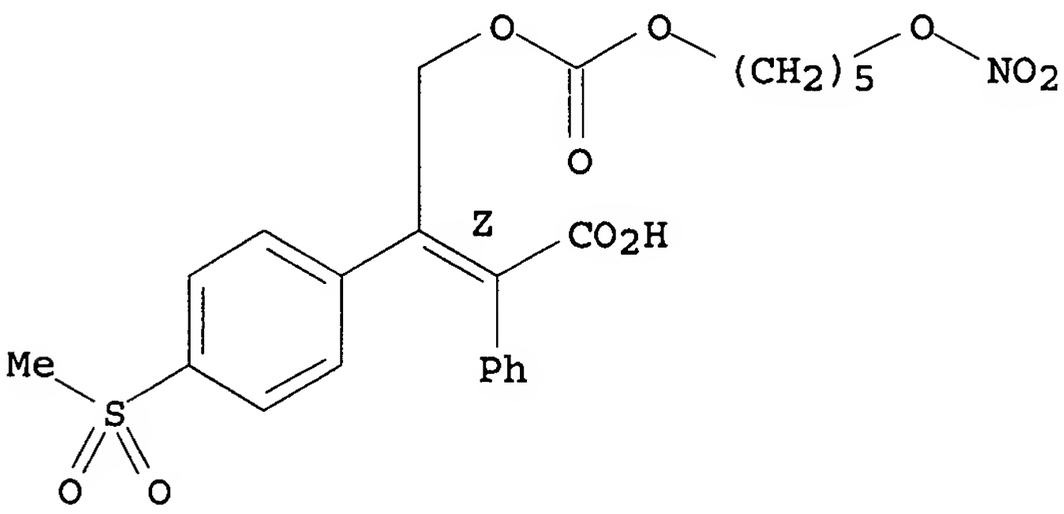
Double bond geometry as shown.



● HCl

IT 654069-07-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of nitric oxide releasing diarylfuranone prodrugs as selective cyclooxygenase-2 inhibitors for treatment of inflammatory diseases)
RN 654069-07-5 CAPLUS
CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[[[5-(nitrooxy)pentyl]oxy]carbonyl]oxy]ethylidene]-, (αZ)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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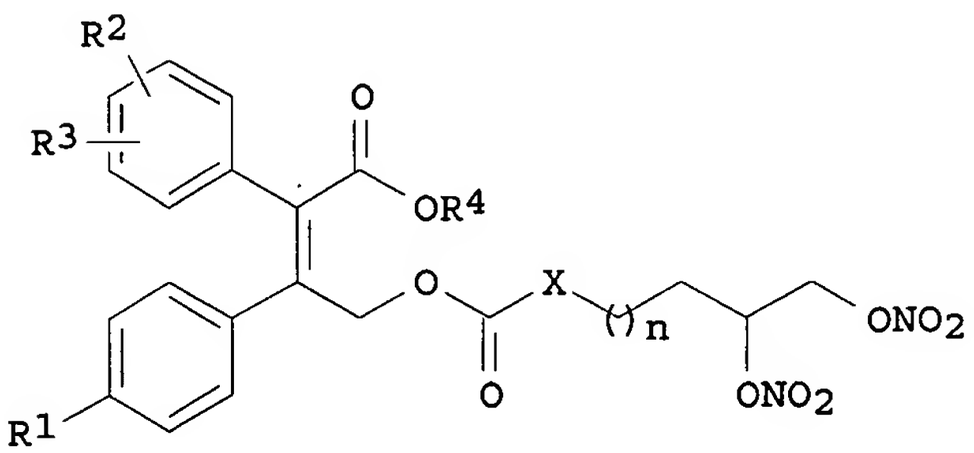
L14 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:696873 CAPLUS
DN 143:172624
TI Preparation of nitric oxide releasing prodrugs of diaryl-2(5H)-furanones as cyclooxygenase-2 inhibitors
IN Dufresne, Claude; Berthelette, Carl; Li, Lianhai; Guay, Daniel; Gallant, Michel; Lacombe, Patrick; Aspiotis, Renee; Wang, Zhaoyin; Sturino, Claudio F.
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005070883	A1	20050804	WO 2005-CA83	20050125

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2004-539666P P 20040127
OS MARPAT 143:172624
GI



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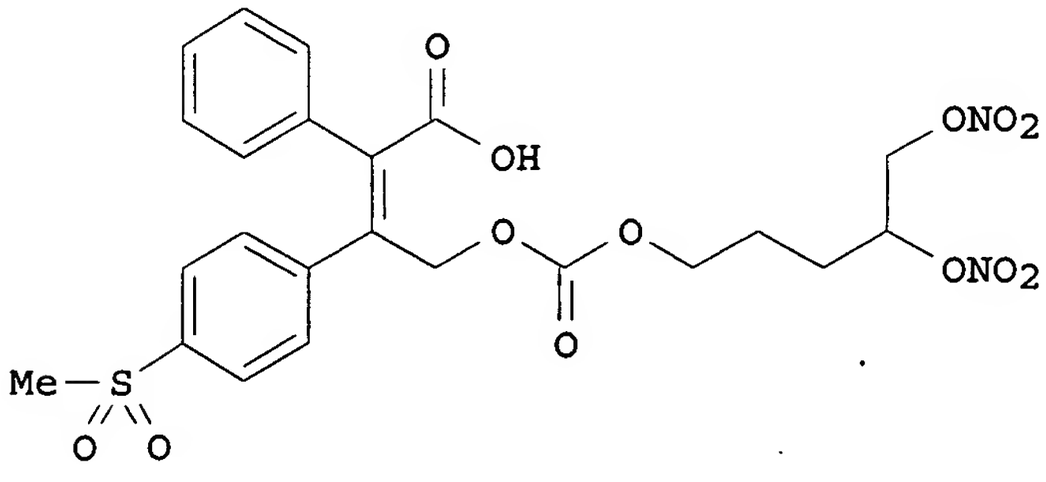

II

AB Nitric oxide-releasing prodrugs I [X = O, CH2; n = 1-6; R1 = SO2CH3, SO2NH2; R2-3 = H, halo, alkoxy, etc.; R4 = H, alkyl, etc.] are prepared For instance, II is prepared in several steps from 3,4-bis(nitrooxy)butyl alc., phosgene and (Z)-4-[(tert-butyldimethylsilyl)oxy]-2-[4-(methylsulfonyl)phenyl]-3-phenylbut-2-en-1-ol. I are useful for the treatment of cyclooxygenase-2 mediated diseases alone and in combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases or conditions while also reducing the risk of thrombotic cardiovascular events [no data].

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:696865 CAPLUS
DN 143:193802
TI Preparation of nitric oxide releasing prodrugs of diaryl-2(5H)-furanones as cyclooxygenase-2 inhibitors
IN Berthelette, Carl; Li, Lianhai; Beaulieu, Christian; Wang, Zhaoyin; Sturino, Claudio F.
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005070874	A1	20050804	WO 2005-CA84	20050125

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2004-540101P P 20040127
OS MARPAT 143:193802
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [n = 1-6; R1 = SO2CH3, SO2NH2; R2-3 = H, halo, alkoxy, etc.; R4 = alkyl, Ph, etc.] are prepared For instance, II is prepared in several steps from 4-(4-(methanesulfonyl)phenyl)-3-phenyl-5H-furan-2-one and hex-5-en-1-ol. I are nitric oxide-releasing prodrugs of diaryl-2(5H)-furanones useful in the treatment of cyclooxygenase-2 mediated diseases [no data]. I may also be used as a combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases or conditions while also reducing the risk of thrombotic cardiovascular events.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:739958 CAPLUS
DN 141:260542
TI Preparation of nitric oxide releasing prodrugs of diaryl-2-(5H)-furanones as selective cyclooxygenase-2 inhibitors
IN Berthelette, Carl; Li, Lianhai; Sturino, Claudio; Wang, Zhaoyin
PA Can.
SO U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004176331	A1	20040909	US 2004-790288	20040301
	AU 2004240700	A1	20041202	AU 2004-240700	20040301
	CA 2517490	AA	20041202	CA 2004-2517490	20040301
	WO 2004103955	A1	20041202	WO 2004-CA314	20040301
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	EP 1601644	A1	20051207	EP 2004-761562	20040301
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PRAI	US 2003-452124P	P	20030305		
	WO 2004-CA314	W	20040301		

OS MARPAT 141:260542
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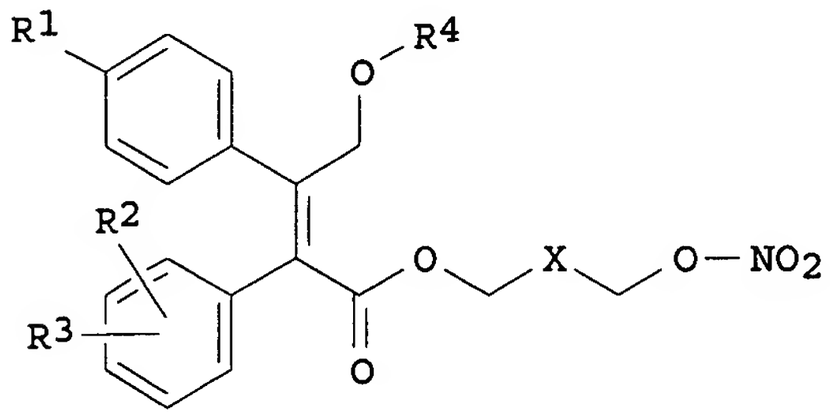

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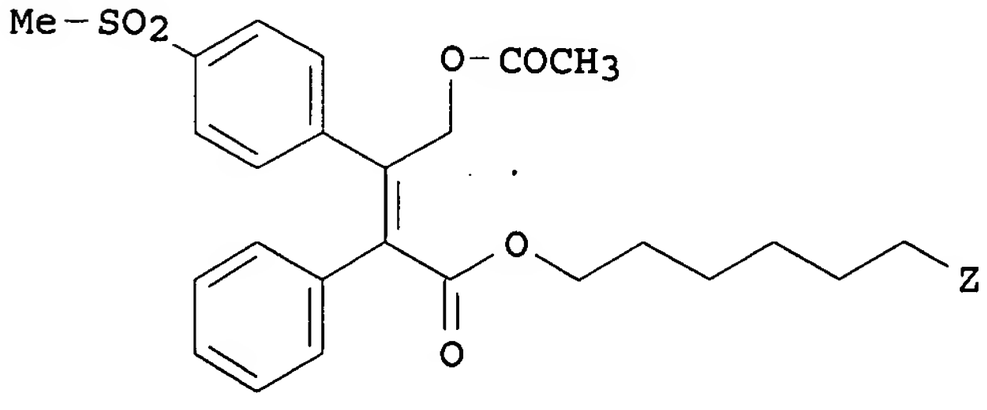

II

AB Title compds. I [X = (CH2)n; n = 3-6; R1 = SO2Me, SO2NH2, SO2NHCOCF3, etc.; R2, R3 = H, halo, alkoxy, etc.; R4 = CO-alkyl, CO(CH2)mNR5R6; m = 1-4; R5, R6 = H, halo-substituted alkyl] and their pharmaceutically acceptable salts were prepared For example, O-alkylation of AgNO3 by bromide II (Z = Br), e.g., prepared from Rofecoxib in 6-steps, afforded nitrooxyhexyl II (Z = -ONO2). In human blood PGE2 inhibition production assays, nitrooxyhexyl II (Z = -ONO2) exhibited an IC50 value of 0.22 μM. Of note, the "unconverted prodrugs" of compds. I are inactive inhibitors of COX-1 and COX-2 activity. Compds. I are claimed useful for the treatment of cyclooxygenase-2 mediated diseases or conditions.

L14 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:412933 CAPLUS
DN 140:423574
TI Preparation of nitric oxide releasing prodrugs of diaryl-2-(5H)-furanones as cyclooxygenase-2 inhibitors
IN Young, Robert N.; Wang, Zhaoyin
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004041803	A1	20040521	WO 2003-CA1691	20031103
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003283096	A1	20040607	AU 2003-283096	20031103
PRAI	US 2002-423866P	P	20021105		
	WO 2003-CA1691	W	20031103		

OS MARPAT 140:423574
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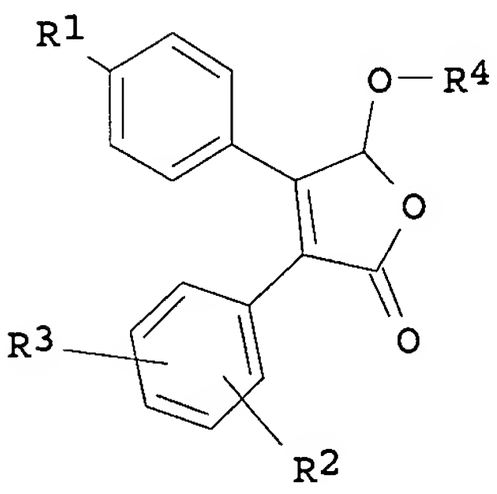

I

AB The title compds. I [R1 = SO2Me, etc.; R2, R3 = H, halo, etc.; R4 = NOm, etc.; m = 1 or 2] are prepared The above compds. may be used as a combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases while simultaneously reducing the risk of thrombotic cardiovascular events.

L14 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:370913 CAPLUS
DN 140:375166
TI Preparation of nitric oxide releasing selective cyclooxygenase-2 inhibitors
IN Wang, Zhaoyin; Young, Robert N.; Zamboni, Robert
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004037798	A1	20040506	WO 2003-CA1605	20031021
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	AU 2003278039	A1	20040513	AU 2003-278039	20031021
	EP 1562914	A1	20050817	EP 2003-769122	20031021
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	US 2006058363	A1	20060316	US 2005-530214	20050404
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OS MARPAT 140:375166
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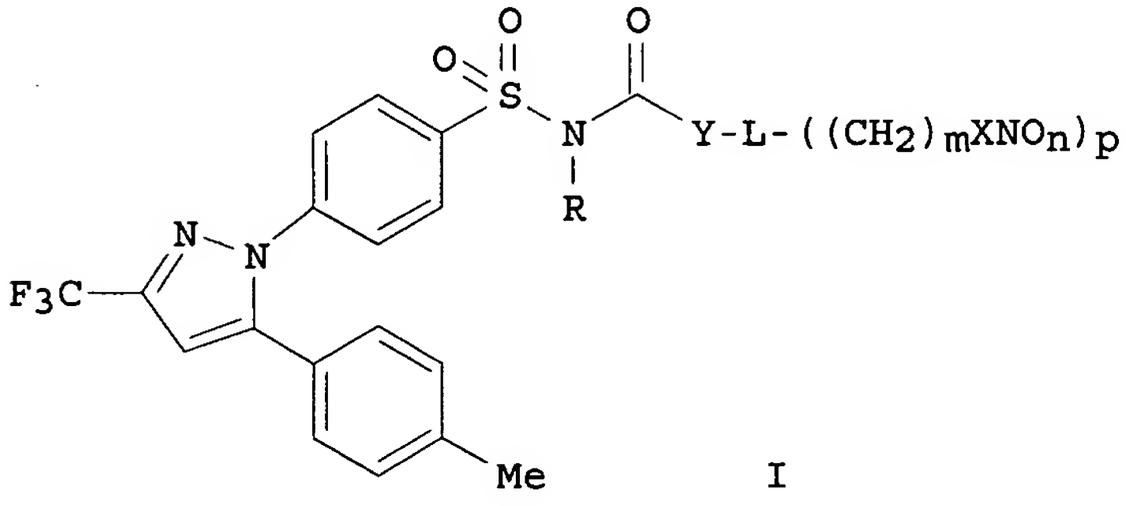

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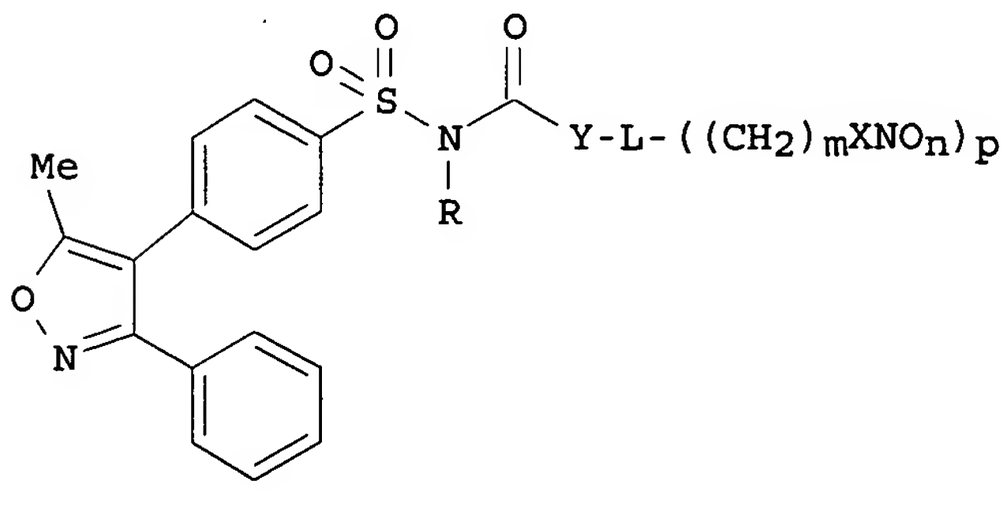

II

AB Novel compds. of formulas I and II [R = H, alkyl; L = bond, alkylidene, cycloalkylidene, aryl, etc.; X = O, S; Y = bond, S, O, (substituted) NH; m = 0-4; n = 1-2; p = 1-4] are prepared, which are nitric oxide-releasing prodrugs useful in the treatment of cyclooxygenase-2 mediated diseases. The invention also encompasses certain pharmaceutical compns. and methods for treatment of cyclooxygenase-2 mediated diseases comprising the use of compds. I or II. The above compds. may be used as a combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases or conditions while simultaneously reducing the risk of thrombotic cardiovascular events.

L14 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:101124 CAPLUS
DN 140:163574
TI Preparation of nitric oxide releasing diaryl-2-(5H)-furanone prodrugs as selective cyclooxygenase-2 inhibitors for treatment inflammatory diseases
IN Berthelette, Carl; Lachance, Nicholas; Li, Lianhai; Sturino, Claudio; Wang, Zhaoyin; Young, Robert N.; Dufresne, Claude
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004011421	A1	20040205	WO 2003-CA1115	20030724
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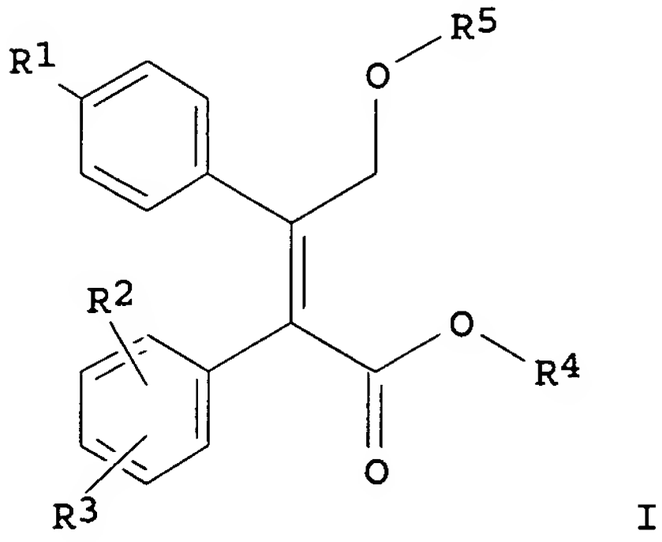
	AU 2003252515	A1	20040216	AU 2003-252515	20030724
	EP 1527045	A1	20050504	EP 2003-771010	20030724
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2005261245	A1	20051124	US 2005-521075	20050112
PRAI	US 2002-398683P	P	20020726		
	US 2002-435341P	P	20021220		
	WO 2003-CA1115	W	20030724		

OS MARPAT 140:163574
GI



I

AB Title compds. I [R1 = S(O)2CH3, S(O)2NH2, S(O)2NHC(=O)CF3, etc.; R2, R3 = H, halo, alkoxy, etc.; R4 = H, (un)substituted alkyl, e.g., halo, Ph, naphthyl, etc.; R5 = NOx, C(=O)-E-alkyl-W-NOx, C(=O)-E-alkyl-Ar-alkyl-W-NOx; x = 1, 2; E = bond, O, S, etc.; W = O, S, C[CO2Rb]2; Ar = (un)substituted Ph, naphthyl, HET3; HET3 = benzimidazolyl, benzofuranyl, benzopyrazolyl, etc.; Rb = (un)substituted alkyl, Ph, naphthyl, etc.] and their pharmaceutically acceptable salts were prepared For example, allylic

bromination of Me (2E)-3-[4-(methylsulfonyl)phenyl]-2-phenylbut-2-enoate, e.g., prepared from 1-(4-methanesulfonylphenyl)ethanone in 2 steps, followed by O-alkylation of AgNO3 afforded nitrate ester I [R1 = 4-S(O)2CH3; R2, R3 = H; R4 = CH3; R5 = NO2] in 23% overall yield. In human whole blood LPS induced PGE2 and TXB2 production assays, compds. I have a COX-2 potency and COX-2/COX-1 selectivity comparable to rofecoxib. In paw edema assays in rat, compound I [R1 = 4-S(O)2CH3; R2, R3 = H; R4 = CH3; R5 = CO2(CH2)4ONO2] exhibited 42-79% inhibition of pain at 1-30 mg/kg dosage. Of note, compds. I are prodrugs of rofecoxib analogs and are claimed useful for the treatment of chronic COX-2 mediated diseases, while reducing the risk of thrombotic cardiovascular events. Compds. I are useful for treatments of osteoarthritis, rheumatoid arthritis, and chronic pain.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d his full

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L4             22 SEA SSS FUL L1 OR L2

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                  D 1-6 BIB ABS


     FILE HOME

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     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

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     DICTIONARY FILE UPDATES:  13 AUG 2006  HIGHEST RN 901009-82-3

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     TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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     predicted properties as well as tags indicating availability of
     experimental property data in the original document.  For information
     on property searching in REGISTRY, refer to:

     http://www.cas.org/ONLINE/UG/regprops.html
```

FILE CAPLUS

FILE COVERS 1907 - 14 Aug 2006 VOL 145 ISS 8
FILE LAST UPDATED: 13 Aug 2006 (20060813/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

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